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14. ABSTRACT

The effects of physical exercise, antioxidant supplementation, and acclimatization on balance were studied during a 13-day exposure of 12 volunteers to 4,300 m altitude. Balance was measured at sea level and altitude, before and after cycle exercise, in subjects receiving either an antioxidant/placebo supplement. Exercise consisted of cycle ergometry at 55% of sea-level maximal oxygen uptake and at the same relative intensity at altitude. Balance was measured using an unstable circular platform system for 3 30-second periods: eyes open, eyes closed, or during random dynamic movement. Acute Mountain Sickness was quantified using the ESQ questionnaire. No differences were found between the placebo and antioxidant groups. No decrement in balance was found within several hours of altitude exposure. There was a trend toward worse balance after 24 h, but by day 6, balance had improved beyond the best sea-level score. Post-exercise balance was only impaired after several hours of exposure. Although the progression of AMS severity showed classic changes, no strong correlation was found between posturographic modalities and AMS.

15. SUBJECT TERMS
altitude, balance, postural stability, antioxidant, physical exercise, acclimatization, acute mountain sickness

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EFFECT OF HIGH ALTITUDE EXPOSURE, ANTIOXIDANT SUPPLEMENTATION, AND EXERCISE ON POSTURAL STABILITY

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July 2006

DISCLAIMERS

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BACKGROUND

This report describes the results of a field study performed during the last year of a 3-yr VA/DoD project designed to study the effects of energy deficit on work performance at 4,300 m elevation (USARIEM H02-01, HSRRB A11189). The project was a multidisciplinary study that allowed several sub-studies to be conducted concurrently without compromising the primary objectives. The primary objectives were to determine 1) if increased levels of physical activity and antioxidant supplementation will affect the incidence, severity, and duration of Acute Mountain Sickness, markers of oxidative stress and immunity, and variables associated with altitude acclimatization; and 2) if carbohydrate supplementation during prolonged exercise will result in improved performance. Descriptions of the study design, volunteer recruitment, and measurement of energy deficit, exercise protocols, and biochemical studies are contained in USARIEM Technical Report No. T-03/07, "Carbohydrate Supplementation Improves Time-trial Cycle Performance at 4300 m Altitude" (12). This study was conducted by investigators and staff from the Thermal and Mountain Medicine Division of the U.S. Army Research Institute of Environmental Medicine and the Geriatric Research, Education and Clinical Center of the Palo Alto Veterans Administration Health Care System.

The sub-study reported here was in partial fulfillment of the requirements of Ms. Kimberly Stone's Human Biology Honors Thesis Project at Stanford University. It was funded, in part, by the Human Biology Department at Stanford University.

ACKNOWLEDGMENTS

EXECUTIVE SUMMARY

Hypoxia caused by rapid travel to high mountain areas can have devastating effects on the health and performance of sensitive individuals. To better understand the factors involved in these detrimental effects, in 2002, the Palo Alto Veterans Affairs Hospital (PAVA) and the United States Army Research Institute of Environmental Medicine (USARIEM) culminated a 3-yr study entitled "Effect of energy deficit on work performance at 4,300 m elevation." The overall goal was to determine the effects of energy deficit, antioxidants, and carbohydrate supplementation on acute mountain sickness (AMS) and physical work performance during acclimatization to 4,300 m. A substudy, incorporated into the main design, investigated the relationship between postural stability (balance), altitude exposure, exercise, and antioxidant supplementation.

Balance was measured at sea level (SL), during acute exposure to altitude (4,300 m), and after acclimatization (2 wk), both before and after high intensity exercise in 12 subjects receiving either an antioxidant supplement consisting of a mixture of β-carotene, α-tocopheral, ascorbic acid, selenium, and zinc, or a placebo. Exercise at sea level consisted of cycling on a stationary cycle ergometer at 55% of their sea-level maximal oxygen uptake and at altitude at the same relative intensity. Cycling was terminated when subjects achieved a level of work equivalent to 40% of their caloric intake. Volunteers' postural stabilities were measured using an unstable circular platform balance system, where deviations from the horizontal were measured continuously for three 30-sec periods in which subjects maintained their balance with their eyes open or closed, or during a dynamic session in which they were asked to rotate the platform in order to follow a random visual pattern. AMS was quantified using the ESQ questionnaire.

No differences were found between the placebo and antioxidant groups in any of the variables measured. This study was the first to describe postural stability with 2 wk of altitude exposure. No decrement in balance ability was found within several hours of altitude exposure. There was a trend toward worse balance control on all 3 modalities (eyes-open, eyes-closed, and dynamic) after 24 h. It was apparent that by Day 6 of continued exposure, postural stability had improved significantly, even beyond the best sea-level score. Improvement was possible due to both acclimatization and continued earning. Even though the workload was adjusted to account for the decrement in maximal performance at altitude, post-exercise balance was only impaired after several hours of exposure. Although the progression of AMS severity showed classic quantitative and temporal changes with altitude acclimatization at 4300 m, no strong correlation was found between the measured posturographic modalities and AMS.

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INTRODUCTION

MILITARY RELEVANCE AND HYPOTHESES

Deployments to high altitude challenge both the physical and mental capacities of Soldiers who must perform at their peak almost immediately. The hostile altitude environment has an immediate, direct impact and a secondary, indirect medical consequence, both of which combine to degrade physical and mental performance. The combined effects are usually transitory if the altitude exposure is not too great and there is sufficient time for natural acclimatization to occur. Physical work and routine tasks are perceived to be more difficult even though the amount of oxygen consumed for a given absolute amount of work remains the same as at sea level. Coupled with the direct effect of hypoxia on mental and physical function, secondary processes culminating in the development of Acute Mountain Sickness (AMS) are invoked that can add to the decrement in performance. If AMS is present, almost all tasks become more difficult and lengthy.

In 1999, the Palo Alto Veterans Affairs Hospital (PAVA) and United States Army Research Institute of Environmental Medicine (USARIEM) began a 3-yr collaborative project entitled "Effect of energy deficit on work performance at 4,300 m elevation." The title of the 3rd summer's study was "The effect of increased energy expenditure, antioxidant intervention, and carbohydrate supplementation on work performance and acclimatization to 4,300 m altitude." Under this rubric, a substudy was designed to investigate the relationship between postural stability (balance), acute mountain sickness, exercise, and antioxidant supplementation.

EXERCISE, ANTIOXIDANTS, AND ACUTE MOUNTAIN SICKNESS (AMS)

Balance/Postural Stability

Postural stability may be impaired by both exercise and the hypoxia associated with altitude exposure. Postural stability is a neuromuscular function controlled by the central and peripheral nervous system and involves input into the central nervous system from the visual, proprioceptive, vestibular, and somatosensory systems (7, 22, 24, 26). Balance is maintained via continuous-loop afferent and efferent nerve pathways that relay signals to stabilizing muscles surrounding joints. The complicated mechanisms involved in maintaining postural stability, including these multiple feedback and regulatory loops, make balance stability susceptible to disturbance and disruption. For example, following exercise, stabilizing muscles are fatigued, diminishing their capacity to maintain stability (9, 10, 22, 24). At altitude, direct and indirect effects of hypoxia on oxygen sensitive areas of the central nervous system may also affect postural stability (5, 14).

AMS, Exercise, and Postural Stability

Dizziness/lightheadedness and fatigue are indicators of hypoxia and impairments in mental and psychomotor function and also serve as subjective indices of the severity of AMS. These symptoms are included in the 11 items used for calculating the severity of the cerebral form of AMS (30). Obviously, these symptoms can also affect postural stability. Several studies have also demonstrated deleterious effects of altitude exposure on balance. These decrements in postural control with altitude exposures can occur as low as 2,440 m (hypobaric hypoxia) and as high as 6,100 m (gas mixtures) (11, 25, 25). The influence of AMS on these observations is probably nonexistent, because the durations of hypoxic exposures on these two studies were on the order of minutes rather than the hours necessary for AMS to become evident. We have shown that postural stability is adversely affected after several hours of acute exposure to 4,300 m simulated altitude, but we could not demonstrate a correlation with the severity of AMS (7).

The situation becomes more complicated when exercise is involved, since initial exposures to altitude are usually associated with relatively moderate exercise and fatigue, at least under field conditions. The combination of exercise/fatigue and hypoxia could combine to additively or synergistically worsen postural stability. It is known that exercise exacerbates AMS (29). Fatigue caused by lower extremity exercise has also been shown to detrimentally affect postural stability and possibly contribute to increased risk of injury (10, 24).

Antioxidants and AMS

Free radicals are highly reactive molecules that can result in damage to stable lipids, proteins, and DNA when produced in excess. Several studies have shown increases in free radical production when elevated oxygen consumption is involved (6, 8, 19, 20). Secondary factors associated with exercise such as lactate production, elevations in core temperature, increased catecholamine release, tissue damage and inflammation, and transient hypoxia with reoxygenation are also thought to increase the production of reactive oxygen species during and following exercise (1, 21). In addition, there is recent evidence that not only are reactive oxygen species increased during both acute (48 h at 4300 m) and chronic altitude (high-altitude residents) without exercise (18), but during the acclimatization process the an adaptive response to oxidative stress could be evoked by activating an antioxidant defense (32).

Several years ago, Bailey et al. (1, 2) proposed that the development of AMS, as well as the early onset and severity of fatigue associated with exercise at altitude, was thought to involve an increase of free radical-mediated changes in vascular permeability and a subsequent inflammatory response. Recent findings, however, have raised doubts as to the importance of the free radical contributory role (3, 4, 17). Nevertheless, there is no question that high-altitude exposure increases oxidative stress, as indicated by increased levels of markers of lipid peroxidation (31). With the administration of supplemental antioxidants that are effective in reducing free radicals, subjects receiving a supplement could demonstrate improved postural stability and an improvement in AMS symptoms if the increase in free radical formation was involved..

There have been no studies that investigate postural stability before and after exercise at high altitude, with and without an antioxidant-supplemented diet.

GOALS

The goals of this investigation were to:

1. test whether a dietary antioxidant vitamin supplementation was associated with changes in postural stability;
2. determine whether changes in postural stability correlated with AMS severity;
3. determine whether postural stability was affected by prior exercise at altitude;
4. determine whether there was an interaction of antioxidant supplementation, exercise, and postural stability at altitude.

METHODS

STUDY DESIGN AND PIKES PEAK ASCENT

As part of a research protocol (H02-01) investigating the effect of increased energy expenditure, antioxidant supplementation, and carbohydrate ingestion on work performance and altitude acclimatization to 4,300 m altitude, 18 healthy male volunteers[*] (mean 25 yr old: range 19-33 yr old) were recruited from the vicinity of Palo Alto, CA, during January through April 2002. Requisite inclusion criteria were 18-35 yr old, non-smokers, normal height-to-weight ratios (body mass index = 20-27), no large weight changes within the last 6 mo, born below 5000 ft (~1,530 m, Denver, CO), residence at or near sea level for 6 mo prior to the study, no ingestion of non-approved vitamins and food supplements, and ability to perform cycle exercise for at least 1 h at ~ 75% of their age-predicted maximal heart rate. All volunteers passed physical exams to include blood and urine analyses.

The first of 3 study phases was a 3-wk stabilization period in which subjects were asked to stop taking any dietary or nutritional supplement for 2 wk prior to the sea-level phase (Figure 1). During the last week of stabilization, the amount of physical activity was controlled, and subjects were fed a controlled diet in order to establish the number of calories necessary for weight stabilization and to control the amount of antioxidants ingested through food. Subjects used the stabilization period to continue learning and practicing.

For the last 5 days of sea-level collection (Baseline), subjects slept in the Clinical Studies Unit of the PAVA, continued to consume the established amount of food, regulated their activity, and performed baseline testing procedures. Subjects were then matched based on their VO_{2peak} (peak oxygen uptake) body composition, end-tidal CO_2, and hypoxic ventilatory response, and randomly assigned to either the placebo or antioxidant group. The antioxidant supplementation (Neutraceuticals©) provided a daily

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[*] Only men were included in the main study, because the antioxidant properties of estrogen could confound the objective of determining the effect of antioxidant supplementation on oxidative stress markers during exercise at altitude.

dosage of 20,000 IU β-carotene, 400 IU α-tocopheral, 500 mg ascorbic acid, 100 µg selenium, and 30 mg zinc. Supplementation was provided for 3 wk prior to ascent and during the first 12 exposure days.

Figure 1. Testing timeline for sea-level and altitude phases

A   Sea-level Phase (Baseline Measurements)
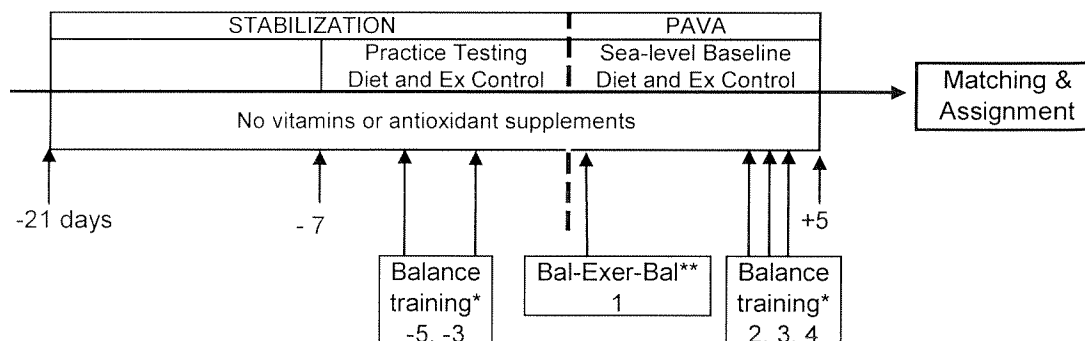
B   High Altitude Phase
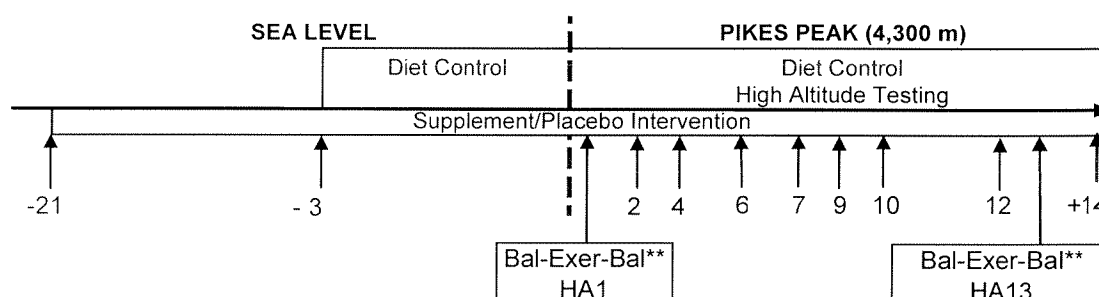
* Training over 2 days at least 5x/day.
** Balance testing occurred before and after the OSI exercise test. See methods for a description of the OSI. exercise test.

Every 1-3 days of July and August 2002, one or two subjects were flown to Colorado Springs, CO (~1,800 m), where they spent the night and early morning on supplemental oxygen supplied by an oxygen concentrator (AirSep, Buffalo, NY) in order to maintain sea-level blood oxygen saturation. During the 1.5-h ascent by automobile the next morning to the US Army Maher Memorial Altitude Laboratory, Pikes Peak, CO (4,300 m), subjects breathed from bottled 100% oxygen. Subjects removed their oxygen masks upon commencing the balance test and the oxidative stress exercise test (OSI, see below for a description). Subjects remained on the summit a total of 14 days (Altitude phase). Conditions at the summit within the USARIEM Maher Memorial Laboratory averaged 460 ± 2 mmHg, 20°-22°C and 15%-20% relative humidity.

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INSTRUMENTATION

All volunteers performed a cycle VO_{2peak} test using an incremental, progressive cycle exercise bout to volitional exhaustion. $VO_{2\ peak}$ was assessed on an electromagnetically braked cycle ergometer (Excalibur Sport, Lode Medical Technology, Gronigen, Netherlands) on Day 3 of the stabilization period, Day 2 of the baseline period, and on altitude Days 2 and 9. Volunteers pedaled at 70-100 rpm for 2 min at 50 W, 2 min at 100 W, and 2 min at 150 W, followed by 30 W increases every 2 min until exhaustion. Oxygen uptake was measured using CHECK PUNCTUATION... indirect calorimety (TrueMax 2400), metabolic cart (ParvoMedics, Salt Lake City, UT), and heart rate via a heart rate watch (UNIQ-CIC, Computer Instruments Corp., Hempstead, NY).

Postural instability was assessed using a computer-controlled unstable platform balance system (K.A.T. 2000, O.E.M. Medical, Carlsbad, CA) that consisted of a 60-cm circular platform (15 cm above the floor), whose ease of tilting was controlled by varying the pressure in a pneumatic bladder situated around a central pivot point. Bladder pressure was adjusted for each subject depending on ambient pressure and subject weight. A balance index score was automatically derived from a tilt sensor that measured the absolute distance between the tilted position and a reference point. The balance index score was thus inversely proportional to balancing skill. A handrail was situated approximately 45° to the left and right of the subject's midline.

Subjects performed 3 different 30-sec balance tests that they had practiced previously. They performed each test barefoot (or in socks) with their arms akimbo and their feet approximately 25 cm apart, equidistant from the central pivot point. They received computer feedback by way of a moving 'X' that indicated the degree of platform tilt, and could control the oscillations by keeping the platform as stable as possible (eyes-open static test). In the second test, with their feet in the same position, the subject repeated the same test with his eyes closed or wearing a blindfold (eyes-closed static test). The third test was dynamic in nature. With both feet positioned as before, the subject was asked to tilt the platform in a direction so as to "chase" a computer-controlled moving ball.

Figure 2. Representation
of the K.A.T. balance system
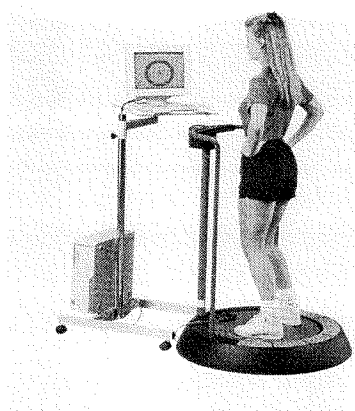
During the stabilization period, subjects were taught how to use the balance platform (Figure 2). On Days -5 and -3 of the diet stabilization period, subjects practiced each of the 3 balance tests at least 5 times, or until they felt comfortable with the tests. On the first day of sea-level baseline period, subjects' balance was tested before and after an amount of cycle exercise designed to induce oxidative stress (OSI test). For the OSI test at sea level, subjects were required to expend 40% of their daily caloric intake (~1,400 kcal) during cycle ergometry at 55% of their $VO_{2\ peak}$. Then, on Days 2, 3, and 4 of sea-level baseline, the subjects performed each balance test 3 times, totaling 15 times per test at sea level. During altitude exposure, the OSI test was adjusted to the

same relative work intensity by reducing the absolute workload 25% to account for the approximately 25% decrease in VO_{2max} (13). At altitude, the subjects performed the balance test before and immediately following the OSI test on Days 1 and 13 and also on Days 2, 4, 6, 7, 9, 10, and 12.

The severity of AMS was assessed using a weighted average score of selected cerebral symptom determined from the Environmental Symptoms Questionnaire (ESQ). The ESQ is a validated, self-reported, 67-question symptom inventory used to determine the presence and severity of symptoms due to exposures to heat, cold, and hypoxia (30). A weighted factor score of 11 subjective symptom scores was used; a value of 0.7 or greater was indicative of the presence of AMS.

STATISTICS

The baseline value used for comparisons to altitude was the "best" or lowest score on each test attained during the sea-level phase. Similarly, at altitude each test was performed 3 times at every time point, and the best (and again lowest) of these scores was used for analysis. The rationale was that low scores could result from lack of effort or distraction, but the best score reflected the volunteer's "true best." Scores obtained during the stabilization period were considered practice.

Repeated measures ANOVA and Fisher's LSD post-hoc analysis (Statistica©, StatSoft, Inc., Tulsa, OK, and Excel©, Microsoft, Redmond, WA) were used to make comparisons between sea-level and acute exposure, acute and chronic altitude, before and after high intensity exercise, and antioxidant versus placebo for all time points. The criterion for statistical significance was a p value of ≤ 0.05. All data are reported as means $\pm$ SE.

RESULTS

COLLAPSED GROUPS

Complete postural and exercise data were collected from 12 trained male subjects: aged 25.1±1.5 yr, weight 77.8±2.9 kg; body fat percent 8.6±1.1%; and V O_{2peak} 54.2±1.7 ml·kg^{-1}·min^{-1} ($\overline{X}$±SE). No significant differences were found between antioxidant and placebo groups in any of the 3 balance measurement conditions (eyes open, eyes closed, and dynamic) regardless of the altitude exposure time (Figure 3). Therefore, all the subjects were combined into 1 group.

Figure 3. Mean balance scores grouped by placebo and antioxidant supplement

Eyes Open

Eyes Closed

Dynamic
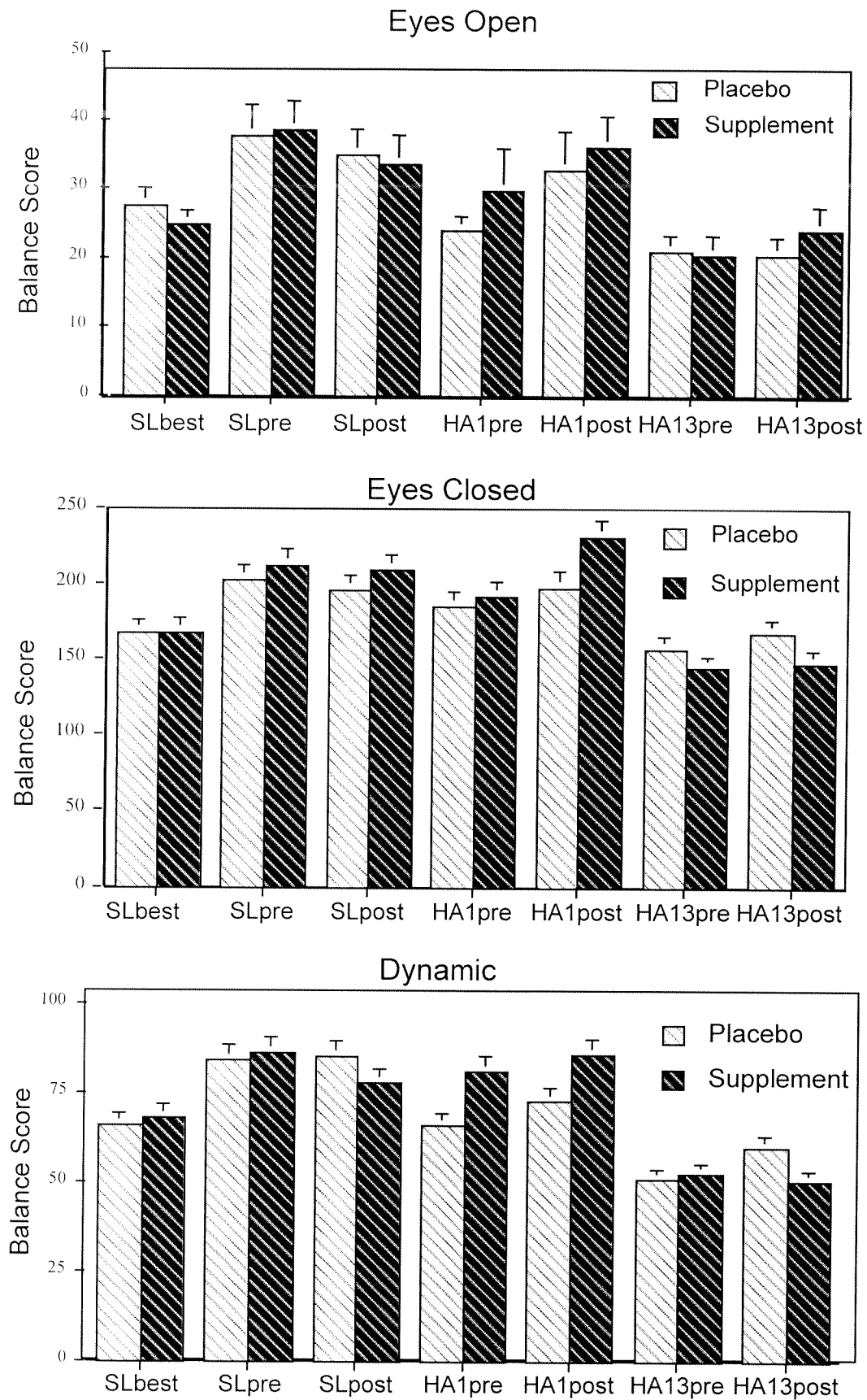
LEARNING EFFECT

Throughout the sea-level stabilization and baseline periods, subjects demonstrated a learning effect in balance ability by improving postural stability (decreasing balance scores). No scores obtained during the stabilization period were used for statistical analyses. All subjects achieved their best sea-level score during the last 3 days of baseline collection. Therefore, the SL-best score for all subjects was significantly better than the SL pre-OSI score, which was measured on Day 1 of stabilization (Figure 4).

At sea level, balance after the OSI exercise (post) was not significantly different than before exercise (pre) for any subtest (EO, EC, and dynamic) (Figure 4). However, in comparison to SL-best, SL post-OSI was significantly worse for all subtests, where a higher score signifies worse balance (Figure 4).

Figure 4. Mean postural stability scores during sea-level testing
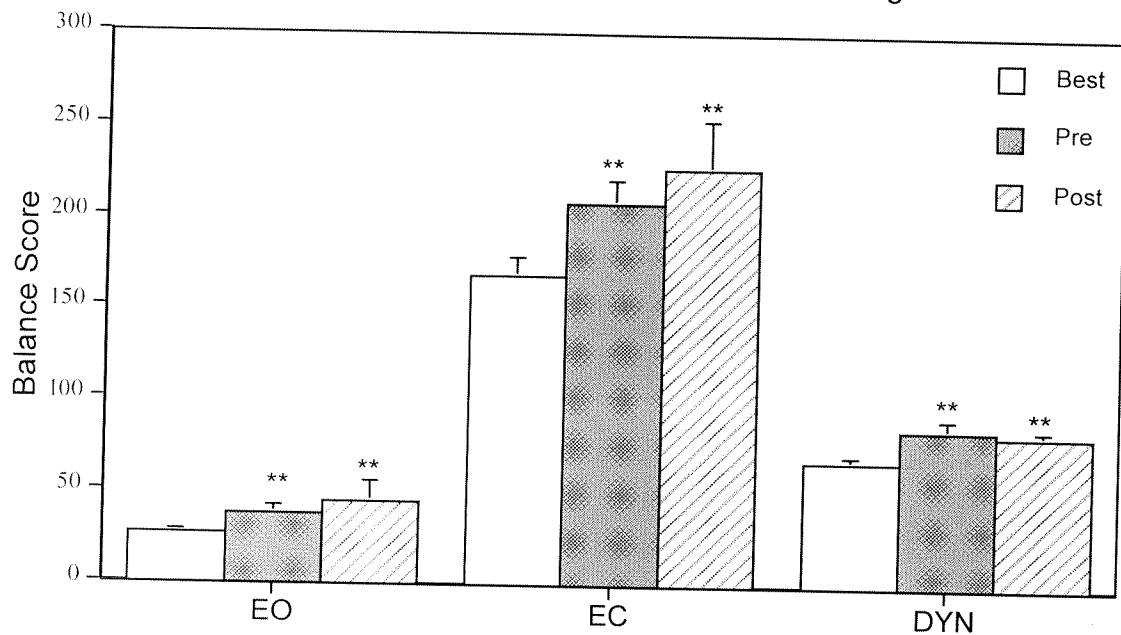
n=12. Best = subjects' best sea-level balance score. The lower the balance score, the better the subjects' postural stability. Pre and Post represent scores before and after the OSI exercise test. Values are mean ± S.E. EO = eyes open; EC = eyes closed; DYN = dynamic. **Significantly different from sea-level best score (p ≤ 0.05).

Upon acute altitude exposure, stability before exercise was not significantly worse than it was before exercise at sea level (Figure 5). In fact, it tended to be better than the sea-level best score on all 3 modalities. On Day 1 of altitude (HA1), all post-exercise balance scores were significantly worse than before exercise, showing that exercise impaired balance upon acute exposure to high altitude. After exercise at altitude, balance decreased by 26% in the EO subtest, while the EC and DYN tests were 14% and 8% worse, respectively (i.e., higher balance scores)(Figure 5).

After 13 days of altitude exposure, significant improvements were shown in all subtests (Figure 5). On HA13, all pre-exercise balance scores were significantly better then both SL best and HA1 pre-exercise. Exercise did not impair balance after chronic altitude exposure, as shown by the fact that post-exercise was not significantly different than pre-exercise.

The trend for all 3 modalities was a slight impairment of balance on altitude Day 1, followed by gradual but statistically significant improvement over the next 12 days at altitude (EO $p<0.05$; EC and DYN $p<0.0001$). A large component of this improvement was likely due to a learning effect. By Day 6 of altitude, the scores for all balance modalities were significantly better than the SL best scores (Figure 6).

There were two exceptions to the general trend. First, the eyes closed score was significantly worse than SL best on altitude Day 2 (HA2), probably due to increased AMS symptoms after the first 12 h ($p<0.01$) (Figure 7). A positive correlation was in fact found between cerebral AMS and loss of balance on HA2 in the morning and evening (Figure 5). Secondly, on altitude Day 7, the eyes closed score was significantly worse than both HA6 and HA9, and the eyes open score was slightly worse, though not significantly.

Figure 8 depicts the changes in cerebral AMS, as measured by the ESQ-C questionnaire. During the first 3 days of altitude exposure, there was a significant increase in AMS symptoms followed by a progressive reduction over the next 11 days. Data reflect the 18 subjects who participated in the main study.

Figure 5. Balance scores in 3 modalities (eyes open, eyes closed, dynamic) before and after exercise at sea level and at 1 and 13 days at 4,300 m
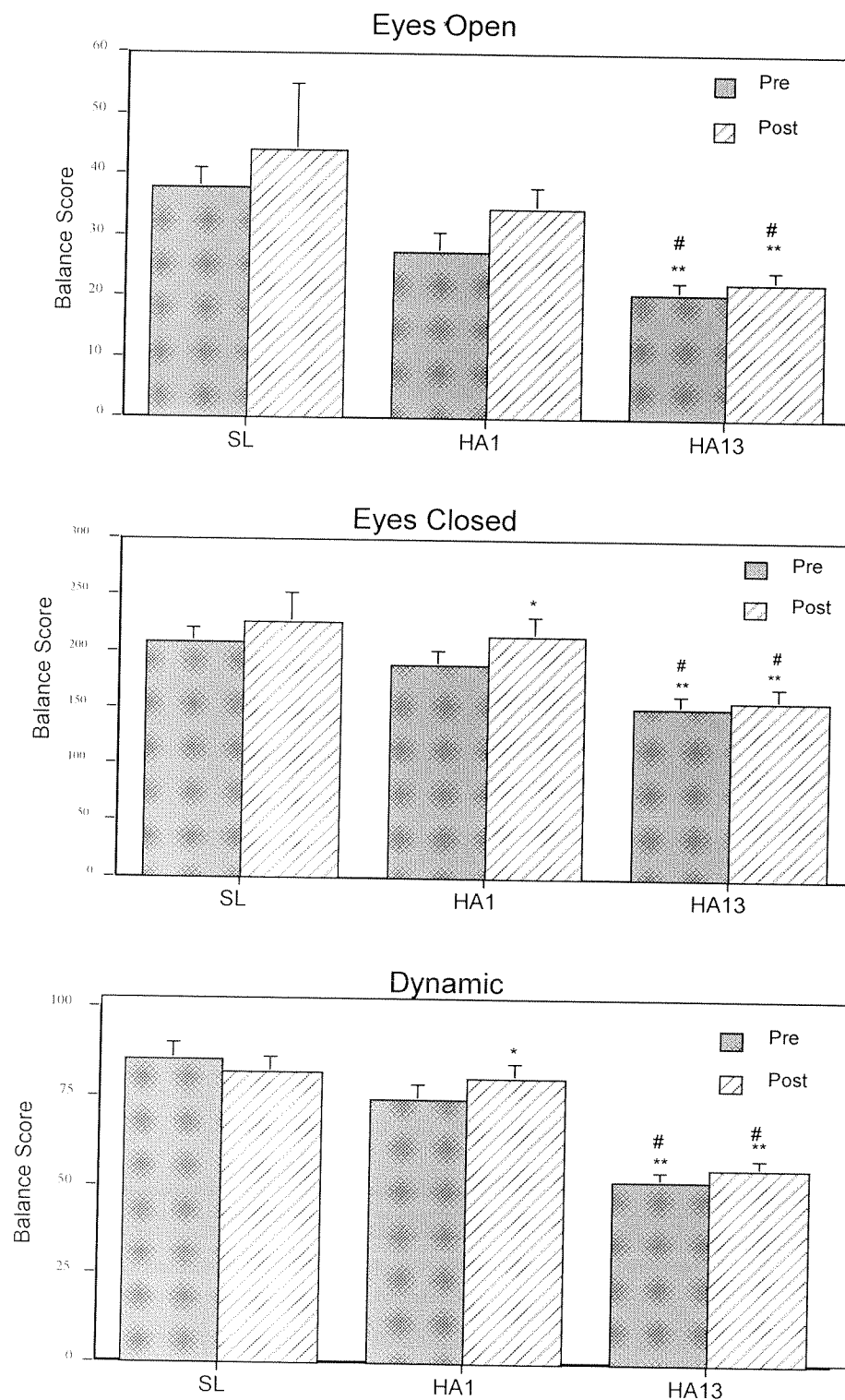
Pre = before exercise; post = after exercise.
SL = sea level; HA1 = Day 1 at 4,300 m; HA13 = Day 13 at 4,300 m.
*P<0.05 from pre; **P<0.05 from sea-level best; #P<0.05 from HA1.

Figure 6. Mean pre-exercise balance scores for the 3 modalities on all test days
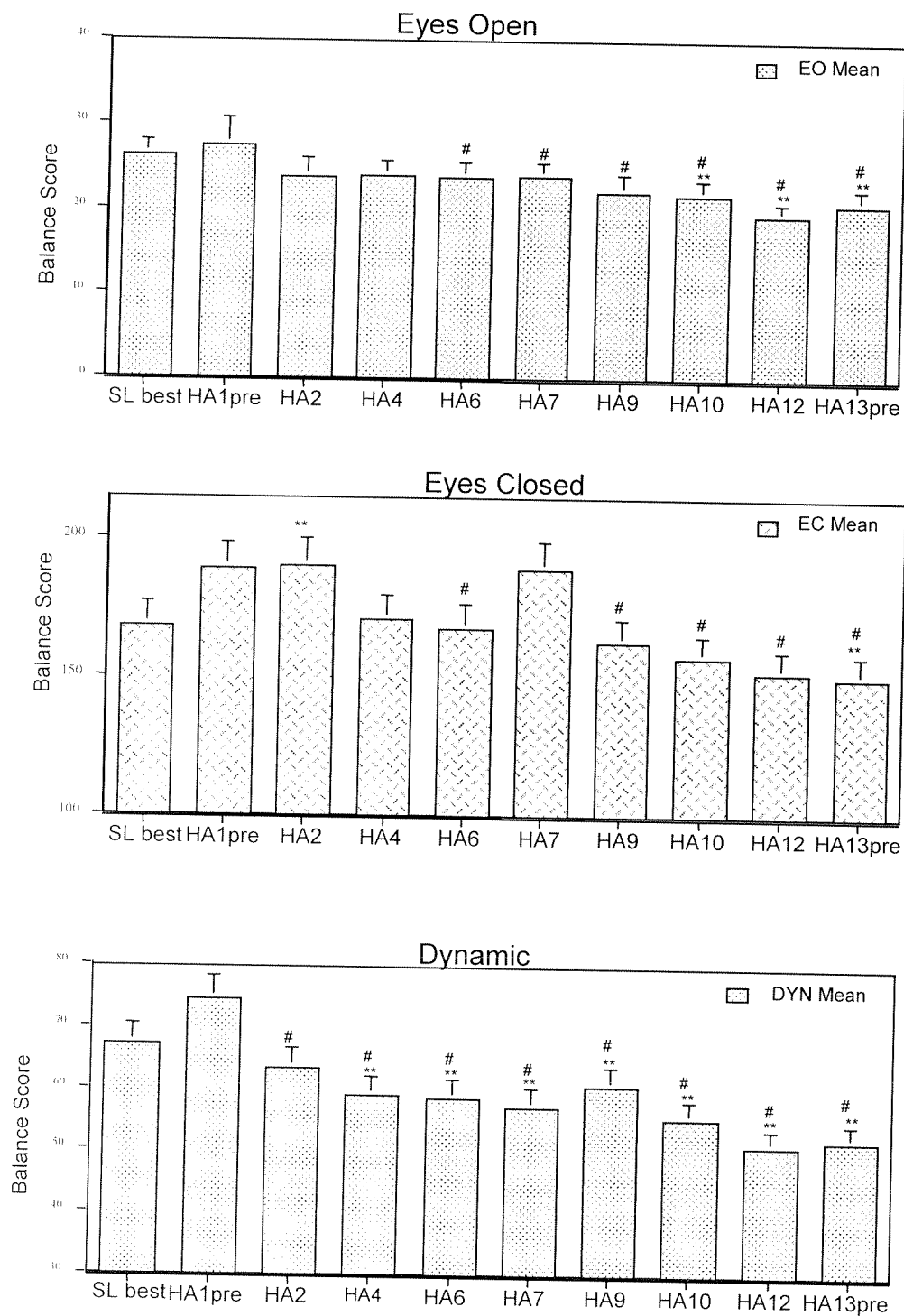
**P<= 0.05 compared to SL best; #P<= 0.05 compared to HA1, the first day at 4,300 m. All data are pre-exercise values.

Figure 7. Correlation of Acute Mountain Sickness severity and the loss of postural stability in the eyes-closed modality on the morning of HA 2 (24 h)

$y = 14.689x + 2.060$

$r = 0.523$
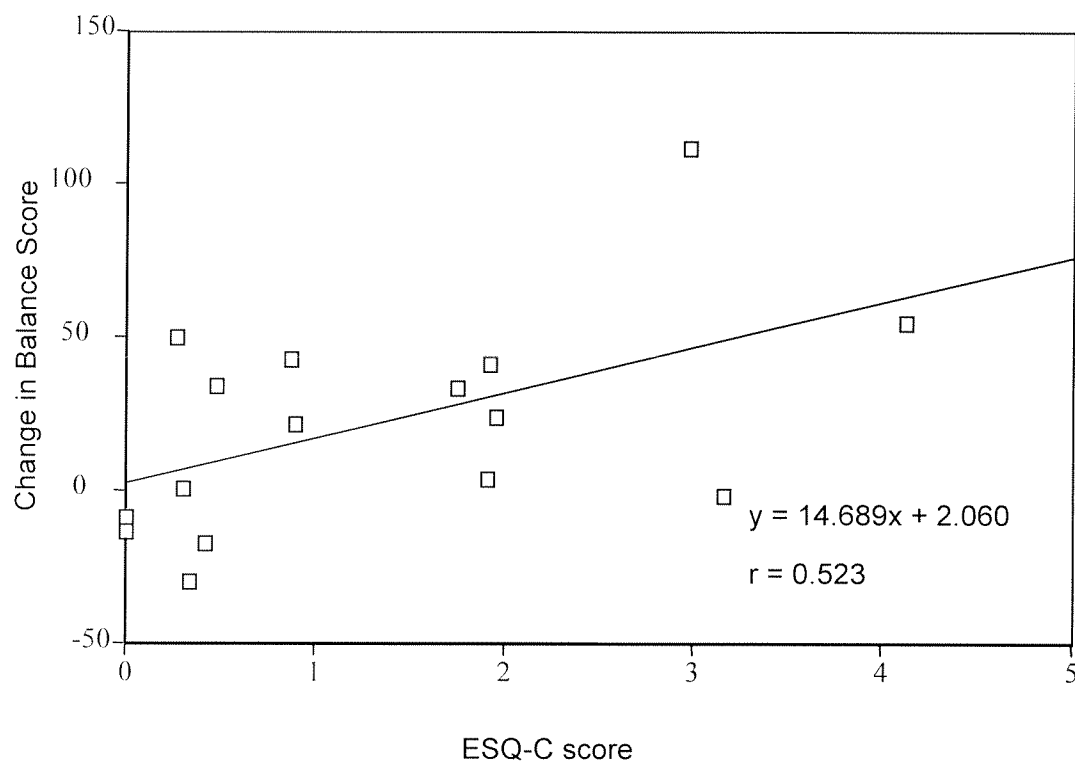
Figure 8. Morning Acute Mountain Sickness (AMS) measured by the ESQ-C during acclimatization to 4,300 m
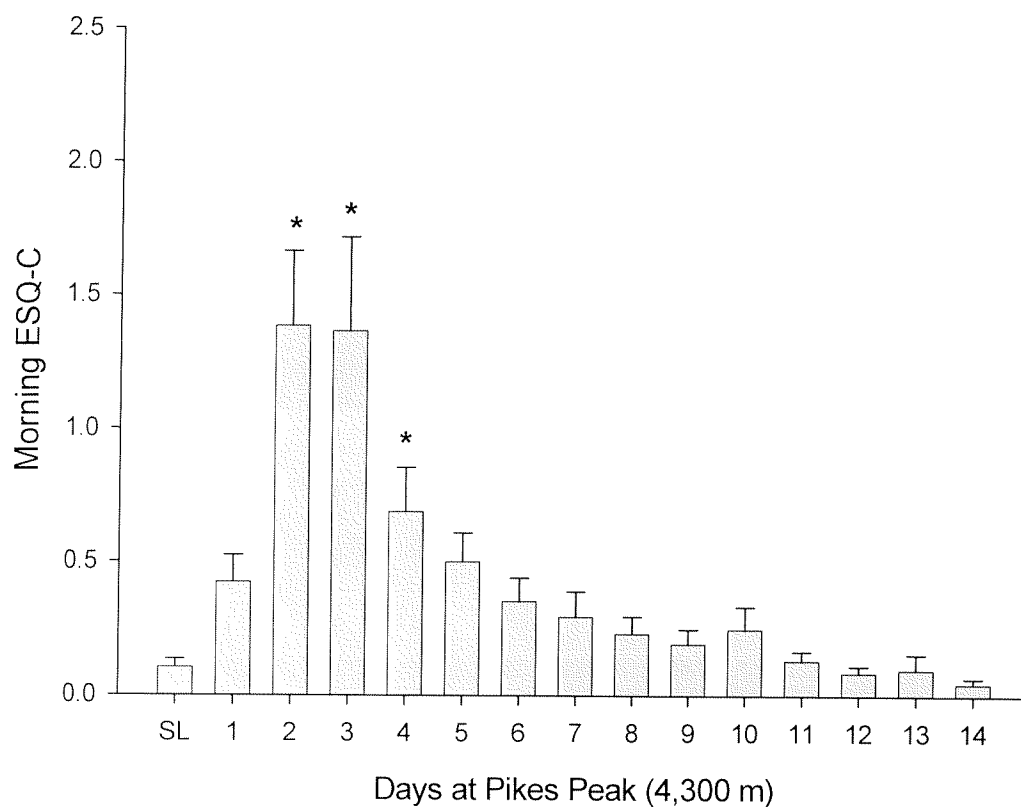
*P < 0.001, means ± SE, n = 18 (< 6 days); n = 17 (> 5 days). Day 1 = ~1 h after removal of supplemental O_2, which was administered during ascent and initially on the Pikes Peak summit. Day 2 and thereafter are progressive 24-h increments.

DISCUSSION

The objectives of the present report were to determine whether 1) antioxidant supplementation would reduce any deleterious effects of altitude exposure on balance; 2) postural stability changes during altitude acclimatization; and 3) postural stability at sea level and altitude would be worse after a moderate degree of cycle exercise. In order to accomplish these objectives, it was necessary to fully acquaint and train volunteers in the balance measurements, testing before and after a specific amount of cycle exercise, and periodically before any exercise during altitude acclimatization.

During the week preceding the sea-level practice measurements and the 5-day period of baseline measurements, volunteers performed the balance procedure a maximum of 20 times. It was our contention that this number of balance tests at sea level was sufficient to accomplish a plateau in training without inducing a further significant learning effect indicative of an improvement in balance. Measurements of "best" performance at sea level were used as representative of a volunteer's balance ability and served as the basis for statistical analyses.

ANTIOXIDANT ADMINISTRATION

There was no significant effect between the antioxidant and the placebo groups at any time, allowing us to combine data from all the subjects into 1 group, thus increasing the statistical power to determine any relationship between AMS and postural stability and the effect of altitude acclimatization.

POSTURAL STABILITY AND ALTITUDE ACCLIMATIZATION

No decrement in balance ability was found within several hours of altitude exposure. The pre-exercise balance score on HA1 (after 2-3 h of exposure) was not significantly worse than either the sea-level best or sea-level pre-exercise scores, but there was a trend toward worse balance control on all 3 modalities; with the eyes-closed and dynamic modalities almost attaining significance ($p= 0.07$ and 0.06, respectively). However, after 24 h (HA2) balance scores for the eyes-closed modality did peak (i.e., decreased stability) (Figure 6) and were significantly worse than SL and HA1 pre-exercise ($p<0.05$).

With continued altitude exposure, it was apparent that by Day 6 of altitude exposure, postural stability had improved significantly in the eyes-open and eyes-closed modalities. With the dynamic modality, significant improvement in balance occurred even earlier, with improvements in scores occurring by HA2 (24 h of exposure). Similar results were obtained in a previous study where decrements in stability showed under the eyes-open and eyes-closed modalities after 3 h, as well as after 24 h of simulated altitude exposure (7). The fact that the latter study was performed using a hypobaric chamber may account for the fact that significance was found after 3 h in the eyes-open modality. Several studies have indicated that there are observed differences between field and chamber studies, with chamber exposures evoking different and possibly more severe responses (23, 27, 28). Other factors may also come into play.

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Volunteers may be better able to "get their bearings" in a natural, more open environment, as opposed to a chamber. Fraser et al. showed worse balance after 30 min of simulated altitude exposure at 5,000, 8,000, and 10,000 feet, but not at 12,000 feet (11). They proposed that there is a coping mechanism that only becomes effective at this higher altitude. However, this does not seem like a plausible explanation, and there are no corroborating studies. Fraser et al. also used the modified Romberg test, which is performed with eyes closed and feet aligned heel to toe. This is a more challenging test than the one we used, and perhaps more sensitive for detecting impairment in balance. Holness et al. investigated whether the rate of onset of hypoxia affected balance using eyes-open and eyes-closed tests (16). Using gas mixtures of 10% and 90% and short exposure times (<10 min), they found that rapid onset hypoxia induced a greater anteroposterior sway than slow-onset, especially when visual cues were eliminated. There are too many differences in methods and procedures between the above studies and ours to conclude that very acute hypoxia adversely affects postural control.

This study is the first to follow balance changes over an extended period of time at altitude. The results showed that with time, subjects were able to improve their scores even beyond their best sea-level score. Balance scores were better than sea level by Day 6 of high altitude and continued to improve, indicating that the improvement may have been part acclimatization and part learning. Despite continued acclimatization, we believe that there was a significant learning effect that was not anticipated. Overall, balance was slightly worse on Day 1 at altitude, but improved throughout the 13 days to become better than the sea-level best.

AMS AND POSTURAL STABILITY

The time interval between removing the supplemental oxygen supply after the subjects arrives at the Pikes Peak summit and balance testing was too short for AMS to be a factor in the balance measurements made during the first time period. The first balance test was administered between 2-3 h after arrival, and AMS symptoms are usually not evident until at least 4-6 h of exposure. However, a significant correlation (r = 0.5) was found between the cerebral score of AMS and the loss of balance measured on HA2 (24 h). This correlation was only shown after 24 h of altitude for the eyes-closed test, and most likely is the most sensitive of the 3 balance tests. After 24 h, the subjects that reported mild cerebral AMS (score <0.5) had already begun to improve their balance scores in the eyes-open and dynamic modalities. Because vision has a primary role in maintaining postural stability, its importance is increased when the other sensory input may be compromised, thus making the blindfolded test modality the most susceptible to impairment.

Although the progression of AMS severity showed classic quantitative and temporal changes with altitude acclimatization at 4300 m, a strong correlation with the measured posturographic modalities was not found. In a previous study, we were able to show that within 24 h, although 63% of the subjects exposed to simulated 4,300 m altitude had significant AMS and there were also increases in postural instability compared to sea level, a correlation between the two was not found (7). Therefore, based on the latter and the present study, we conclude that acute altitude, simulated or

real, has an immediate, deleterious effect on postural stability, that the effect lasts at least 24 h, and that there is no direct relationship to AMS severity.

PRE/POST EXERCISE EFFECTS

We initially predicted that balance would be worse after exercise at all time points, but significant differences were found only on HA1. Subjects performed balance tests before and after a heavy bout of exercise on a cycle ergometer at sea level, HA1, and HA13. The goal of the exercise test for each subject was to burn 40% of his daily caloric intake (~1500 kilocalories). In order to achieve this, workload was set so subjects cycled at 55% of their VO_{2max}, as determined during baseline period. We expected impaired balance, based on the findings of previous studies; however, those studies used different protocols, intensities, and types of exercise, which may explain why our results do not confirm their findings.

Derave et al. found that 30 min of treadmill exercise impaired eyes-open balance only, not eyes-closed, and concluded that exercise negatively affects the visual contribution to static postural stability (10). They found no overall pre/post effect on bi-directional postural away, but there was an interaction between vision and locomotion. They performed balance tests in 15-sec intervals and found that the pre/post effect disappeared after 2 min. We saw no difference in balance scores after exercise at sea level or after acclimatization, but there was a decrement after exercise for all modalities on HA1. Other than the immediate effects of hypoxia, there could be several explanations for our lack of a pre/post exercise effect.

The type of exercise performed or the exact timing of the measurements could be a contributory factor. More jarring of the head occurs in treadmill running, causing visual disruption during exercise that can cause instability when testing is performed immediately following completion. During cycling, the head is held in a more constant position with little or no jarring. This could explain why exercise alone did not induce impairment of balance (except on HA1) and why the difference between eyes-open and eyes-closed was not observed in our study. The Derave study (10) showed that the exercise-induced impairment of balance disappeared after 2 min. Similarly, our balance tests were administered between approximately 2-5 min after completion of exercise, and thus may not have shown balance impairment on HA13 and possibly on HA1. Hashiba et al. confirmed the lack of agreement between treadmill and cycle exercise when balance was measured (15). They showed that the vision during treadmill locomotion plays an important role in evoking postural sway after exercise. Of more relevance, Lepers et al. manipulated visual conditions during exercise and balance tests and concluded that balance was impaired after exercise in a visually altered environment, and that balance decreased immediately after running, but to a lesser extent after cycling (22). They also confirmed that running and cycling affect postural stability differently, thereby limiting direct comparisons between studies using treadmill and cycle ergometers.

Derave et al. also found no differences when comparing balance pre-/post-exercise alone, while changes in postural instability were dependent on fluid replacement and corresponding hydration levels following exercise (9). In this study, subjects exercised twice for 2 h, 1 time without drinking and 1 time with drinking a

carbohydrate-electrolyte solution. Postural stability tests were performed 20 min after each exercise session (in a dehydrated and hydrated state), using the eyes-open test and 2 different foot stances. Using subjects' best score, they found balance to be worse when dehydrated. Hydration may have initially played a role in our study as well, as subjects could have been dehydrated on the first day of high altitude due to both altitude-induced diuresis and exercise. By HA13, our acclimatized subjects were probably better hydrated before, during, and after exercise.

At altitude, the workload during the exercise test was adjusted based on a predicted decrease of VO_{2max} of 30% at altitude. The subjects rode at a lower absolute intensity for a longer time at altitude in order to expend the same number of calories. At sea level, the test lasted less than 3 h, and at altitude it lasted up to 4 h. We found that those who struggled with the HA1-exercise test (i.e., had to be given oxygen, a decreased work load, or could not finish the test) had worse post-exercise balance scores on average. On HA13, all subjects reported that the exercise felt easy to moderate, and balance after the test was not significantly impaired. Having acclimatized for 2 wk, subjects felt that the same bout of exercise that was extremely challenging on HA1 was no longer as fatiguing on HA13. The fatigue experienced on HA1 contributed to the loss of balance after exercise, but by HA13 the exercise no longer caused such fatigue, and therefore did not cause imbalance. This conclusion is only partially supported by a study by Nardone et al. who found that fatiguing treadmill exercise increased sway, non-fatiguing exercise induced no change, and fatiguing cycle exercise only elicited negligible change in sway; while non-fatiguing cycle exercise caused no change at all (24).

Unfortunately, Nardone et al.'s comparisons between types of exercise may be questionable because different exercise protocols were used for treadmill and cycle exercise. After the treadmill exercise, subjects stopped abruptly and balance tests were administered 2 min later, after subjects no longer felt dizzy. After cycling, subjects had a cool-down period on the bike, never reported feeling dizzy, and therefore started balance tests about 1 min after cool down. Nevertheless, their conclusion--only fatiguing exercise causes instability--is still noteworthy and can explain why the exercise on HA13 in our study did not cause loss in balance, since it was no longer fatiguing.

When comparing the present results to those in the literature, it appears that number of practice tests, intensity of exercise, exercise on a cycle ergometer versus treadmill, and side-by-side versus heel-to-toe testing might explain many of the differences that were observed pre/post exercise. Even though we found that balance was only impaired after exhaustive exercise at acute high altitude, it is likely that most types of strenuous exercise hamper one's ability to maintain stability. However, more sensitive procedures need to be used to quantify this effect.

CONCLUSIONS

It was hypothesized that antioxidants would reduce AMS symptoms and, therefore, balance would be better with antioxidant treatment. Antioxidants did not reduce AMS, nor did they improve balance. We also predicted that very acute exposure to 4,300 m altitude would impair postural stability. Performance in any of the balance

modalities was not worse before exercise within several hours of exposure, possibly because AMS had not yet developed. Performance on the eyes-closed modality was worse after 24 h, corresponding to a peak in cerebral AMS. It was also hypothesized that acclimatization would restore any loss of balance due to altitude. By HA13, all scores had improved beyond the best scores obtained at sea level, as a consequence of both acclimatization and learning. Since the mechanism for maintaining postural stability includes visual input and the action of stabilizing muscles, it was hypothesized that balance would be impaired after exercise at all measured time points (SL, HA1, HA13). Although the workload was adjusted to account for the decrement in maximal performance at altitude, post-exercise balance was only impaired with acute altitude. Finally, the correlation between symptoms of AMS and postural instability is not sufficient to consider the balance test as a possible tool to predict or diagnose AMS.

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